SYNTHESIS, CHARACTERISATION, ANTIMICROBIAL EVALUATION OF 2-HYDROXY PHENYL THIAZOLIDINE-4-ONE DERIVATIVE

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ABSTRACT

A new series of N-(2-(2-hydroxyphenyl)-4-oxothiazolidin-3-yl) isonicotinamide derivatives were synthesized by the reaction of schiff base (Isoniazid and 2 hydroxy benzaldehyde) with mercaptoaetoc acid respectively. The chemical structures of the synthesized compounds were confirmed by means of IR, 1H-NMR. The synthesized compounds showed good antibacterial activity against Staphylococcus aureus and Escherichia coli.

KEYWORDS: Antibacterial, Aromatic aldehyde, Isoniazid, Schiff Bases, Thiazolidine-4-one.

1. INTRODUCTION

Azetidinone and Thiazolidinone derivatives were reported to possess antibacterial\cite{1,2}, antifungal\cite{1,2}, antitumor\cite{3} antitubercular activity\cite{4}, anti-HIV\cite{5}, analgesic\cite{6}, anti inflammatory\cite{6}, and ulcerogenic activity\cite{7}. Pyridine derivatives were reported to possess antimicrobial\cite{8} activities. Therefore it was envisaged that compounds containing both the chemical moieties would result in compounds of interesting biological activities. In this present study isoniazid was treated with 2-hydroxy benzaldehyde to produce Schiff base\cite{9}. The Schiff bases were subjected to addition reaction with thioglycollic acid in the presence of 1,4dioxane, anhydrous zinc chloride to produce 4-thiazolidinone derivative respectively\cite{10}. The chemical structures of the synthesized compounds were confirmed by means of IR, 1H-
NMR. The synthesized compounds were screened for antibacterial activity against *Staphylococcus aureus, Escherichia coli*.

2. **Chemistry:** The melting points were taken in open capillary tube and are uncorrected. The IR spectra of the compounds were recorded on Win-Bommen B-104 IR Spectrophotometer with KBr pellets. 1H-NMR spectra was recorded on Bruker A VIII 500 MHz NMR Facility using DMSO-d6 as solvent. The chemical shifts are reported as parts per million downfield from tetramethyl silane (Me4Si). The purity of the compounds was checked by TLC on pre-coated aluminium sheets(Silica gel 60 F254) using absolute alcohol :ethyl acetate : Glacial Acetic acid as mobile phase and visualized by iodine vapors Synthetic scheme for Schiff Bases and Thiazolidine-4 one

![Chemical structure](image)

3.1 **General Methods of Synthesis of Schiff Base (S)**

A mixture of Isoniazid (0.01mol), 2-hydroxy benzaldehyde[11](0.01mol) and a drop of acetic acid was dissolved in ethanol (25ml) and heated on a steam bath for 45-60 min or on a water bath for 2-3 hrs. The reaction mixture was allowed to stand at room temperature for 24h,The product separated out was filtered, dried under vacuum and recrystallized by using warm
ethanol. The Schiff bases and thiazolidine-4-one derivatives were prepared by the method of S.Ramachandran et al.,[12,13].

(E)-N’-(2-hydroxybenzylidene)isonicotinohydrazide

IR (KBr) cm⁻¹:3158 (NH), 1673 (C=O, Amide), 1611(C=N), 1274 (C-OH)

General Methods of Synthesis of Thiazolidine-4-one (S1)

To a mixture of schiff base(0.01mol) and thioglycolic acid (0.01mol) dissolved in 1,4 dioxane (20ml), anhydrous zinc chloride (0.004 mol) was added and refluxed for 8hours. The reaction mixture was cooled, filtered, washed with water, vacuum dried and recrystallised using absolute ethanol.

2-((4-(dimethylamino)phenyl)-3-(pyridin-2-yl)thiazolidin-4-one

IR (KBr) cm-1:3429 (NH), 1961(C=O), 1680 (C=O, amide), 1617(C-N), 2920 (C-OH)

1H-NMR
(DMSO-d6) : 7.8-8.9(m, 2H; CH Pyridine ), 6.95-6.98(m, 2H; benzene ) 8.6(s, 1H; CH-benzylidene), 8.3 (s, IH, NH), 3.7 ( aromatic OH) 2.5 (s, 2H; CH2)

3.3 Antimicrobial activity

The antibacterial activity[14] of the synthesised compounds was tested against gram(+) bacteria (Staphylococcus aureus ATCC5144 and gram(-) bacteria (Escherichia coli ATCC 25922 using Nutrient agar medium.

3.4 Cup Plate method[15,16]

Inoculate a previously liquefied medium appropriate to the assay with the requisite quantity of suspension of the micro organism, add the suspension to the medium at a temperature between 40 to 50°C and immediately pour the inoculated medium into petri dishes to give a depth of 3-4mm. Ensure that the layers of medium are uniform in thickness by placing the dishes or plates on a level surface.

The prepared dishes must be stored in a manner so as to ensure that no significant growth or death of the test organism occurs before the dishes are used and that the surface of the agar layer is dry at the time of use. The cavities in the agar plates are prepared be using a metal borer. The cavities formed must be uniform throughout the dish. Apply the solutions to the surface of the solid medium in sterile cavities prepared in the agar medium. The volume of solution added to each cavity must be uniform and sufficient almost to fill those holes when
these are used. Leave the dishes standing for 1-4 hrs at room temperature or at 4°C as appropriate as a period of pre-incubation diffusion to minimise the effects of variation in time between the applications of different solutions. Then the plates are incubated at 37±1°C for 24 hrs and observed for antibacterial activity. The diameter of the zone of inhibition was measured for the plates in which the zone of inhibition was observed. The average area of inhibition in millimetre (mm) was calculated and compared with that of the standards as shown in the Table 1 below.

Table 1: Zone of Inhibition in mm

<table>
<thead>
<tr>
<th>S.No</th>
<th>Compound</th>
<th>Staphylococcus aureus (Gram+ve)</th>
<th>Escherichia coli (Gram -ve)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Zone of Inhibition in mm</td>
<td>Zone of Inhibition in mm</td>
</tr>
<tr>
<td>1</td>
<td>Standard 50 µg/ml</td>
<td>44mm</td>
<td>40mm</td>
</tr>
<tr>
<td>2</td>
<td>Sample S1 100 µg/ml</td>
<td>22mm</td>
<td>29mm</td>
</tr>
<tr>
<td>2</td>
<td>Sample S1 200 µg/ml</td>
<td>24mm</td>
<td>30mm</td>
</tr>
</tbody>
</table>

The antibacterial activity of the Synthesised compound S1 performed using ciprofloxacin as standard. The concentration of ciprofloxacin used was 50 µg/ml and the concentration of synthesises S1 used was 100 µg/ml and 200 µg/ml respectively. The antibacterial activity was done against Staphylococcus aureus (Gram +ve) and Escherichia coli (Gram –ve ). The compound S1 showed mild activity against both the organisms.

4. SUMMARY AND CONCLUSION

The present work describes the synthesis of Schiff bases and their thiazolidinone derivatives along with their antibacterial activities.

The Schiff bases and thiazolidine-4-one derivatives were prepared by the method of S.Ramachandran et al. The reaction completion was confirmed by TLC and the synthesised compounds were purified by recrystallisation.

The structures of the synthesised compounds were assigned on the basis of the spectral data. The infra red, nuclear magnetic resonanace spectra of these Schiff bases and thiazolidinone compounds showed the expected frequencies and signals.
The antimicrobial activity of the thiazolidinone derivatives was screened by the cup plate method with the standard drug ciprofloxacin, control(solvent DMSO) and the samples(Compound S1). It showed that the compound had mild activity both towards gram +ve and gram –ve organisms. The standard used was ciprofloxacin.

6. ACKNOWLEDGEMENT
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5. REFERENCE


